Non-technical abstract

The purpose of this research is to develop a treatment strategy in which patients' own immune system can be stimulated to fight against melanoma in particular and other cancers in general. This treatment strategy involves collecting patients' own dendritic cells (DCs); loading the DCs with genes that produce melanoma proteins (antigens) that are capable of stimulating patients' own killer lymphocytes (white blood cells called cytotoxic T lymphocytes, CTLs), which can travel to the tumor site and kill the melanoma cells. The DCs loaded with the tumor antigens constitute a tumor vaccine. We expect that this strategy will generate much less toxicity than conventional chemotherapy and radiotherapy in the treatment of cancers.

A strategy using similar tumor vaccines loaded with short peptides of a single antigen stimulated CTLs in patients and induced regression of some tumor nodules. Although the results were very encouraging in the sense that cancers can potentially be treated in such a relatively nontoxic and natural way, most of the tumor nodules in that strategy escaped the attacks. We hypothesize that the problem with that strategy was either that different tumor cells bear different antigens, or that not enough CTLs were stimulated.

To circumvent those problems, we have designed our protocol so we will use DCs loaded with enough different antigens to cover the different subsets of melanoma cells while recruiting helper T cells to boost the stimulation of CTLs. We found out that both goals can be achieved by using an engineered equivalent of the genes (RNA) that encode the tumor antigens to load the DCs for CTL stimulation. We call this the RNA-DC type of vaccine.

The main objectives of this study are as follows:

1. To determine the safety and toxicity of the RNA-DC vaccine for melanoma,
2. To identify the doses of the vaccine that effectively stimulate CTLs against multiple melanoma antigens, and
3. To explore the relationship between the stimulated CTLs and the target tumor cells, and
4. To discover the clinical responses to the vaccine.

By conducting this study, we hope to foster further development of immunotherapy, which we believe will eventually lead to benefits for patients with melanoma in particular, and cancer patients in general.